REMARKS

The claims are 45-50 with claim 45 being the sole independent claim. Claims 1-44 have been canceled without prejudice or disclaimer. Support for claims 45-50 may be found throughout the specification and in previously pending claims 1-44. The specification has been amended to include the section heading, Brief Description of the Drawings, and to include a description of Figure 1. Support for this description may be found at page 18, lines 14-15. No new matter has been added.

Claims 22-25, 35-40, and 42 were provisionally rejected on the ground of obviousness-type double patenting being unpatentable over claims 1-3, 7, and 10-13 of copending Application No. 10/502,376 (USAN '376) in view of Glinecke, et al. (WO 00/28990, (WO'990)). Claims 30-34 were rejected under 35 U.S.C. 112, first paragraph, and claims 22-26, 30-40, and 42 were rejected under 35 U.S.C. 112, second paragraph. Claims 22-26, 30-40 and 42 were further rejected as allegedly unpatentable over Staniforth (US 5,004,614) in view of Glinecke, et al. (WO 00/28990) and as allegedly unpatentable over Martini et al. (WO 03/068195) in view of Glinecke, et al. (WO 00/28990).

Applicants respectfully traverse each of these rejections. Cancellation of claims 1-44 renders these rejections moot, however, Applicants will address the rejections to the extent that they apply to claims 45-50.

Double Patenting and Section 103 Rejections

The Examiner made three obviousness-based rejections of the previously pending claims over 1) copending USAN '376, 2) Staniforth and 3) Martini, each in view of Glinecke.

Applicants respectfully submit that the claimed dosage form is distinct from the oral dosage forms claimed in USAN '376 and described in Staniforth and Martini, when viewed in combination with Glinecke. The claimed dosage form contains a unique combination of elements that have been arranged in a novel way.

Applicants respectfully submit that the Examiner is using improper hindsight analysis in making these rejections. The Examiner has provided no explanation, why one skilled in the art – without the benefit of knowledge of the present invention – would be motivated to specifically create a core formulation of 5-[4-[2-(N-methyl-N-(2 pyridyl)amino)ethoxy]benzyl]thiazolidine-2,4-dione maleate or a hydrate thereof

(hereinafter "rosiglitazone") having two separate rosiglitazone-containing compositions that would provide both immediate and delayed release of the rosiglitazone, and provide an enteric coating over that core, and would further provide two holes in the enteric coating and still further provide that the two holes expose each of the immediate release and the modified release compositions of the core to the environment of use (stomach/intestines).

General motivation of "further controlling the dissolution and release of the active agent" is insufficient to support the multiple selections required to construct the claimed dosage form from the multiple dosage form elements described in the cited art.

Specifically, the Examiner has provided no explanation, why one skilled in the art – without the benefit of knowledge of the present invention – would combine the recited elements in the recited manner, with any expectation that such a dosage form would successfully achieve the recited results, that is, to provide for release of rosiglitazone such that the mean maximum plasma level concentration and/or the mean area under the plasma concentration versus time curve over the dosing interval at steady state for rosiglitazone are maintained independent of food intake.

Staniforth

In support of the Section 103 rejection over Staniforth, in view of Glinecke, the Examiner alleges, at page 13, that it would have been obvious to "incorporate a multi-layer tablet....in the controlled release device comprising a core and coating with an opening as taught by Staniforth." At page 14, the Examiner concludes that "the structure recited by the prior art and the claims are the same..." Applicants respectfully submit that Staniforth does not disclose the coating and openings of the claimed dosage form, nor is there any dosage form described or suggested in Staniforth or Glinecke that is the same as the claimed dosage form.

A key aspect of Staniforth is the controlled release of an active agent thru an opening (hole) in an impermeable outer coating, such that the external/environmental fluid does not contact the core except through that opening. It cannot be said that Staniforth merely teaches the use of openings in a coating. Staniforth requires an outer coating that will remain in place during the dispensing period.

Staniforth actually teaches away from the coating present in the claimed dosage form – that is, use of an enteric coating that disintegrates in the pH environment found in the small intestine.

At column 3, lines 46 to 49, Staniforth states:

> The outer coating may be chosen so as to eventually dissolve in the external fluid, or be degraded thereby *after* substantially all of the active agent has been released from the device. *(emphasis added)*

In the claimed dosage form, the presence of an enteric coat provides for the coating to dissolve/disintegrate *during* release of the active agent. Thus, incorporating a selected multi-layer tablet in the controlled release device comprising a core and coating with an opening as taught by Staniforth would not provide a structure that is the same as the claimed dosage form.

USAN '376 and Martini

Applicants note that USAN '376 is the U.S. national phase application corresponding to WO 03/068195 (Martini), thus the double patenting and Section 103 rejections will be addressed together.

Each of Martini and Glinecke independently disclose various compositions that provide modified release of anti-diabetic medicines. Absent hindsight, no reason has been provided as to why one skilled in the art would pick and choose among the numerous dosage forms and dosage form elements disclosed in Glinecke (dosage forms having delayed, pulsed or sustained release, or a combination thereof, using disintegrating, non-disintegrating, or eroding matrices, microparticulates, enteric coatings, semi-permeable coatings, etc.) and Martini to select the compositions and arrangement of those compositions as recited in the pending claims.

At page 17 of the office action, the Examiner further concludes:

> Similarly, because the structure recited by the prior art and the claims are the same, the mean plasma level concentration level of the drug and the mean area under the plasma concentration versus time curve over the dosing interval at steady state will be maintained substantially independent of food during use and the mechanism of release of the drug will be the same.

Applicants respectfully submit that there is simply no support for these conclusions. No dosage form described or suggested in Martini or Glinecke is the same as the claimed dosage form. The mechanisms of release of the drug from the dosage forms of Martini and the various forms disclosed in Glinecke are different. Thus there is no basis to compare the

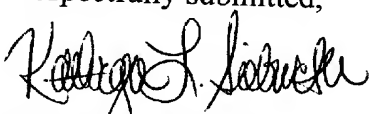
mean plasma level concentrations and/or AUCs of the prior art dosage forms with the claimed dosage form.

The Supreme Court in *KSR* stated that a modification may likely be the product of ordinary skill when it "leads to the anticipated success." As Applicants argued above – without the benefit of knowledge of the present invention – one skilled in the art would not have basis to expect that the claimed dosage form would successfully achieve the recited results, that is, to provide for release of rosiglitazone such that the mean maximum plasma level concentration and/or the mean area under the plasma concentration versus time curve over the dosing interval at steady state are maintained independent of food intake.

For all of the reasons provided above, Applicants respectfully submit that the Examiner has failed to establish a prima facie case of obviousness of the claimed dosage form over the dosage forms claimed in copending USAN '376, and described in Staniforth and Martini, each considered in combination with Glinecke.

In view of the above amendments and remarks, reconsideration of this application is requested. Should the Examiner have any questions or wish to discuss any aspect of this case, the Examiner is encouraged to call the undersigned attorney at the number below.

Respectfully submitted,



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